Atty Dkt. No.: R0130D-CON
USSN: 10/823,012

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this correspondence is being transmitted via facsimile to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA, 22313-1450, at (571) 273-8300, on the date indicated below.

Name of Person Transmitting: Robert C. Hall

Signature:

Date: May 10, 2006

PATENT
Attorney Docket No.: R0130D-CON

DECLARATION OF COUNDE O-YANG (37 CFR §1.132	Attorney Docket Confirmation No.	**R0130D-CON**
	First Named Inventor	**Michael P. Dillon et al.**
	Application Number	**10/823,012**
	Filing Date	**April 14, 2004**
	Group Art Unit	**1626**
Address to: Commissioner for Patents Alexandria, VA 22313-1450	Examiner Name	**Laura L. Stockton**
	Title	**IMIDAZOLINYL ARALKYLSULFONAMIDES**

Dear Sir:

1. I, Counde O-Yang, declare and say I am a co-inventor of the claims of the above-identified patent application. I directed others and/or personally performed the research leading to the invention disclosed and claimed therein.

Unexpected Properties

2. Agonists of the alpha 1A adrenoceptor are recognized in the art as being useful for the treatment of genitourinary indications such as various types of incontinence. Modulation of the alpha 1A adrenoceptor can unfortunately result in blood pressure increase and undesirable cardiovascular side effects. A desirable property in alpha 1A agonists is "uroselectivity", i.e., the ability to affect intraurethral pressure (and hence treat incontincence) while avoiding substantial increase in blood pressure.

3. Both the instant compounds and those of US 5,952,362 have affinity for the alpha 1A adrenoceptor. However, the 2-chloro-4-imidazolinylmethyl (*para)* compound of the above-identified application has unexpectedly better uroselectivity than the analogous 2-chloro-5-imidazolinylmethyl (*meta)* compound of US 5,952,362.

4. In FIG. 1 and FIG. 2 below, there are shown graphical illustrations of the intraurethral pressure (IUP) versus the mean arterial blood pressure (MAP) for *meta* and *para* analogs determined in an *in vivo* anesthetised rabbit model (see Example 8 of US 6,756,395). The vertical axis represents change of pressure from baseline in millimeters of mercury, and the horizontal axis represents dosage (micrograms of drug per kilograms body mass). The IUP values are represented by circles, while MAP values are represented by squares. The triangles and pentagons represent control solution values for MAP and IUP respectively.

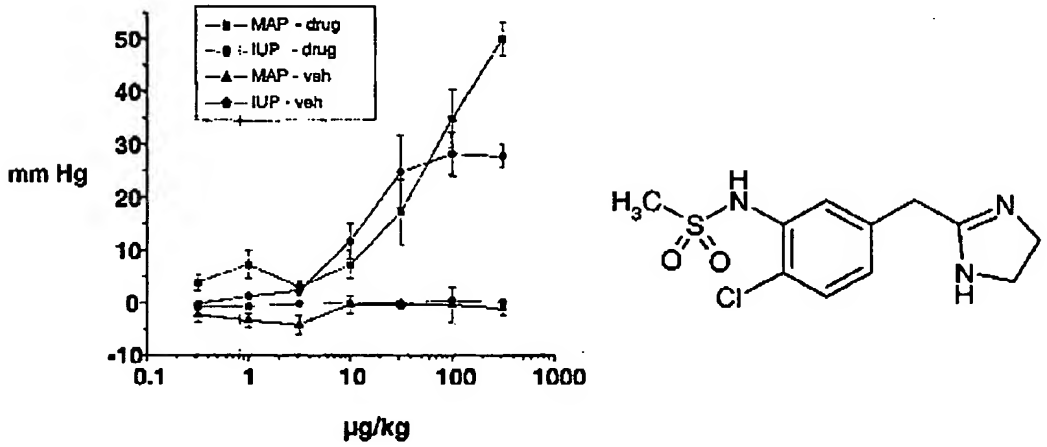

FIG. 1: Intraurethral pressure (IUP) and mean arterial blood pressure (MAP) for N-[2-Chloro-5-(4,5-dihydro-1H-imidazol-2-ylmethyl)-phenyl]-methanesulfonamide (US 5,952,362).

5. As can be seen in FIG. 1, the mean arterial pressure for the *meta* compound increases commensurately with the intraurethral pressure at lower dosage regimens, and substantially exceedes the intraurethral pressure at 100 µg/kg and above. The greater increase in

arterial blood pressure with respect to intraurethral pressure demonstrates absence of urosclectivity in the *meta* compound.

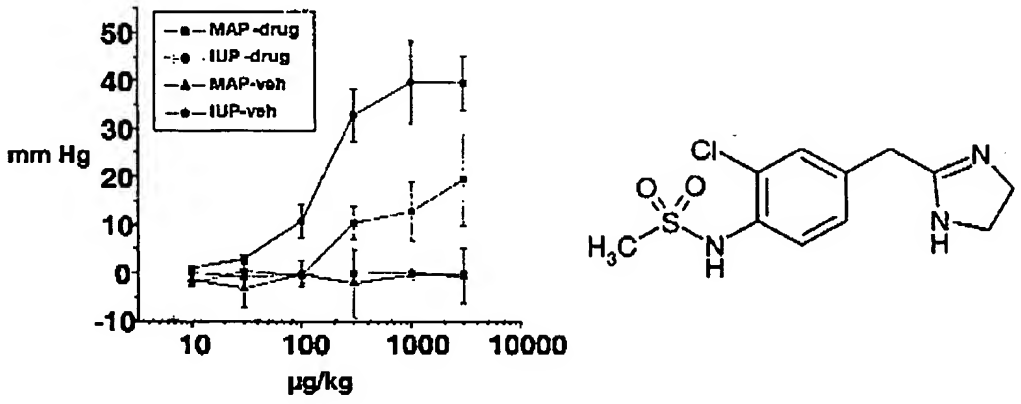

FIG. 2: Intraurethral pressure (IUP) and mean arterial blood pressure (MAP) for N-[2-Chloro-4-(4,5-dihydro-1H-imidazol-2-ylmethyl)-phenyl]-methanesulfonamide

6. In FIG. 2, the intraurethral pressure exceeds the mean arterial pressure at low dosages, and substantially exceeds the mean arterial pressure at at 100 µg/kg and above. The greater increase in intraurethral pressure with respect to arterial blood pressure indicates good uroselectivity in the *para* compound.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title XVIII of the United States Code, and that such will false statements may jeopardize the validity of the application or any patent issuing thereon.

5/10/06
Date

Counde O-Yang

Director of Research, Medicinal Chemistry,
Roche Palo Alto